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Anticancer Activity of Calyx of Diospyros kaki Thunb. through Downregulation of Cyclin D1 Protein Level in Human Colorectal Cancer Cells

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Abstract : In this study, we elucidated anti-cancer activity and potential molecular mechanism of DKC against human colorectal cancer cells. DKC-E70 suppressed the proliferation of human colorectal cancer cell lines such as HCT116, SW480, LoVo and HT-29. Although DKC-E70 decreased cyclin D1 expression in protein and mRNA level, decreased level of cyclin D1 protein by DKC-E70 occurred at the earlier time than that of cyclin D1 mRNA, which indicates that DKC-E70-mediated downregulation of cyclin D1 protein may be a consequence of the induction of degradation and transcriptional inhibition of cyclin D1. In cyclin D1 degradation, we found that cyclin D1 downregulation by DKC-E70 was attenuated in presence of MG132. In addition, DKC-E70 phosphorylated threonine-286 (T286) of cyclin D1 and T286A abolished cyclin D1 downregulation by DKC-E70. We also observed that DKC-E70-mediated T286 phosphorylation and subsequent cyclin D1 degradation was blocked in presence of the inhibitors of ERK1/2, p38 or GSK3β. In cyclin D1 transcriptional inhibition, DKC-E70 inhibited the expression of β-catenin and TCF4, and β–catenin/TCF-dependent luciferase activity. Our results suggest that DKC-E70 may downregulate cyclin D1 as one of the potential anti-cancer targets through cyclin D1 degradation by T286 phosphorylation dependent on ERK1/2, p38 or GSK3β, and cyclin D1 transcriptional inhibition through Wnt signaling. From these findings, DKC-E70 has potential to be a candidate for the development of chemoprevention or therapeutic agents for human colorectal cancer. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2016R1D1A3B03931713).

Keywords : anticancer, calyx of persimmon, cyclin D1, Diospyros kaki Thunb., human colorectal cancer
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